

We Claim:

1. An electronic device for performing active biological operations comprising:

a support substrate,

an array of microlocations disposed on the substrate,

a first collection electrode disposed on the substrate,

first and second focusing electrodes disposed on the substrate, the first and second electrodes being disposed at least in part adjacent the array of

microlocations, the distance between the first and second electrodes adjacent the array being smaller than the distance between the first and second electrodes in

yet another region disposed away from the array, and

counter electrodes disposed on the substrate.

2. The electronic device for performing active biological operations of claim 1 further including at least one transport electrode, the transporting electrodes being disposed on the substrate, and positioned between the first collection electrode and the array.

3. The electronic device for performing active biological operations of claim 2 wherein there are at least two transporting electrodes.

4. The electronic device for performing active biological operations of claim 3 wherein the transporting electrodes are of a different size.

5. The electronic device for performing active biological operations of claim 4 wherein the ratio of larger to smaller is at least 2:1.

6. The electronic device for performing active biological operations of claim 4 wherein the ratio of larger to smaller is at least 3:1.

7 The electronic device for performing active biological operations of claim 4 wherein the ratio of larger to smaller is at least 4:1.

5 8. The electronic device for performing active biological operations of claim 4 wherein the transporting electrodes generally decrease in size the closer then are to the array.

10 9. The electronic device for performing active biological operations of claim 8 wherein the decrease in size is monotonic.

10. The electronic device for performing active biological operations of claim 2 wherein the at least one transport electrode is smaller than the first collection electrode.

15 11. The electronic device for performing active biological operations of claim 10 wherein the ratio of the area of the collection electrode to the transport electrode is at least 4:1.

20 12. The electronic device for performing active biological operations of claim 1 further including capture sequences.

13. The electronic device for performing active biological operations of claim 12 wherein the capture sequences are disposed adjacent the collection electrode.

25 14. The electronic device for performing active biological operations of claim 12 wherein the collection electrode is a complexity reduction electrode.

30 15. The electronic device for performing active biological operations of claim 1 further including a second power supply for connection to the focusing electrodes.

16. The electronic device for performing active biological operations of claim 1 wherein the focusing electrodes are biased negative..

17. The electronic device for performing active biological operations of claim 1 wherein the focusing electrodes are actively biased to zero.

18. The electronic device for performing active biological operations of claim 1 further including a flow cell.

19. The electronic device for performing active biological operations of claim 1 wherein the counterelectrodes and first collection electrodes are disposed for interrogating a substantial fraction of the volume of the flow cell.

20. The electronic device for performing active biological operations of claim 19 wherein the fraction is at least 50%.

21. The electronic device for performing active biological operations of claim 19 wherein the fraction is at least 75%.

22. The electronic device for performing active biological operations of claim 19 wherein the counterelectrodes and the collection electrode are disposed along substantially all of the periphery of the footprint of the flow cell.

23. The electronic device for performing active biological operations of claim 22 wherein the counterelectrodes and collection electrode are disposed along at least 80% of the periphery of the flow cell footprint.

24. The electronic device for performing active biological operations of claim 19 wherein the counterelectrodes and collection electrode are disposed at substantially opposite ends of the flow cell footprint.

25. The electronic device for performing active biological operations of claim 18 wherein the area of the collection electrode and counter electrodes in proportion to the footprint of the flow cell is at least 40%.

5 26. The electronic device for performing active biological operations of claim 18 wherein the area of the collection electrode and counter electrodes in proportion to the footprint of the flow cell is at least 50%.

10 27. The electronic device for performing active biological operations of claim 18 wherein the area of the collection electrode and counter electrodes in proportion to the footprint of the flow cell is at least 60%.

15 28. The electronic device for performing active biological operations of claim 18 wherein the flow cell includes an inlet.

29. The electronic device for performing active biological operations of claim 18 wherein the flow cell includes an outlet.

20 30. A method for analysis of a biological sample, utilizing the electronic device for performing active biological operations of claim 1, comprising the steps of:
providing the sample to the device,
placing the first collection electrode attractive for the desired charged biological materials, thereby concentrating desired charged biological materials on the collection electrode,

25 placing the focusing electrodes at a potential so as to provide a component of force transverse to the line disposed between the collection electrode and the array of microlocations, and

transporting material from the collection electrode to the array of microlocations.

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31. The method for analysis of a biological sample of claim 30 wherein the focusing electrodes are actively biased.

32. The method for analysis of a biological sample of claim 31 wherein the active bias of the focusing electrodes is to zero.

33. The method for analysis of a biological sample of claim 31 wherein the bias is negative.

34. The method for analysis of a biological sample of claim 30 further including the step of providing attractive bias to the transport electrodes relative to the desired sample.

35. The method for analysis of a biological sample of claim 30 wherein the transport electrodes are biased attractive relative to the desired sample material after the desired sample has been provided to the collection electrode.

36. The method for analysis of a biological sample of claim 30 wherein the transport electrodes are sequentially biased.

37. The method for analysis of a biological sample of claim 30 wherein the collection electrode is biased repulsive to the desired sample at a point after the desired materials have been collected at the collection electrode.

38. The method for analysis of a biological sample of claim 30 further including the step of actively biasing at least certain microlocations in the array of microlocations attractive to the desired biological materials.

39. An electronic device for performing biological operations comprising:
a support substrate,

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an array of microlocations disposed on the substrate, the array being formed within a region,

a first collection electrode disposed on the substrate adjacent the array, and

5 a second collection electrode disposed on the substrate, adjacent the array, and at least in part on the opposite side of the region.

40. The electronic device for performing biological operations of claim 39 wherein the first collection electrode and second collection electrode are disposed at
10 substantially opposite ends.

41. The electronic device for performing biological operations of claim 39 further including a flow cell, the flow cell adapted to be supported on the substrate and to define a footprint of the flow cell.
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42. The electronic device for performing biological operations of claim 41 wherein the first collection electrode and second collection electrode are disposed at substantially opposite ends of the footprint of the flow cell.

20 43. The electronic device for performing biological operations of claim 39 wherein the collection electrode has an area at least 80 % of the area of the region.

44. The electronic device for performing biological operations of claim 39 wherein the collection electrode has an area at least 100 % of the area of the region.
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45. The electronic device for performing biological operations of claim 39 wherein the collection electrode has an area at least 120 % of the area of the region.

46. The electronic device for performing active biological operations of
30 claim 39 further including capture sequences.

47. The electronic device for performing active biological operations of claim 46 wherein the capture sequences are disposed adjacent the collection electrode.

48. The electronic device for performing active biological operations of claim 39 wherein the collection electrode is a complexity reduction electrode.

49. The electronic device for performing active biological operations of claim 39 further including focusing electrodes.

50. The electronic device for performing active biological operations of claim 41 wherein the area of the first collection electrode and second collection electrode in proportion to the footprint of the flow cell is at least 40%.

51. The electronic device for performing active biological operations of claim 41 wherein the area of the first collection electrode and second collection electrodes in proportion to the footprint of the flow cell is at least 50%.

52. The electronic device for performing active biological operations of claim 41 wherein the area of the first collection electrode and second collection electrodes in proportion to the footprint of the flow cell is at least 60%.

53. The electronic device for performing active biological operations of claim 41 wherein the flow cell includes an inlet.

54. The electronic device for performing active biological operations of claim 41 wherein the flow cell includes an outlet.

55. A method for analysis of a biological sample, utilizing the electronic device for performing active biological operations of claim 39, comprising the steps of:
providing the sample to the device,

placing the first concentration electrode attractive for desired charged biological materials, thereby concentrating charged biological materials on the concentration electrode,

5 placing the second concentration electrode attractive for the desired charged biological materials, relative to the first concentration electrode, thereby transporting said charged biological materials from the first concentration electrode towards the second concentration electrode, and over at least a portion of said array of microlocations disposed on the substrate, whereby interaction between the charged biological materials and the array occurs.

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56. The method for analysis of a biological sample of claim 55 utilizing an electronic device for performing active biological operations, wherein the array is maintained electrically passive.

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57. The method for analysis of a biological sample of claim 55 utilizing an electronic device for performing active biological operations, wherein the array is electrically active to facilitate interaction between the array and the charged biological material.

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58. The method for analysis of a biological sample of claim 55 utilizing an electronic device for performing active biological operations, wherein the charged biological material is moved over the array as a wave.

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59. The method for analysis of a biological sample of claim 55 utilizing an electronic device for performing active biological operations, wherein the charged biological material is moved over the array.

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60. The method for analysis of a biological sample of claim 55 utilizing an electronic device for performing active biological operations, wherein the charged biological material is moved over the array and maintained in that lateral position relative to the substrate.

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61. An electronic device for performing active biological operations comprising:

a support substrate,

an array of microlocations disposed on the substrate,

a first collection electrode disposed on the substrate surrounding the array, and

a counter electrode disposed on the substrate and disposed interior of the array.

62. The electronic device for performing active biological operations of claim 61 wherein the first collection electrode is segmented.

63. The electronic device for performing active biological operations of claim 61 wherein multiple rings are provided surrounding the array.

64. The electronic device for performing active biological operations of claim 61 further including capture sequences.

65. The electronic device for performing active biological operations of claim 64 wherein the capture sequences are disposed adjacent the collection electrode.

66. The electronic device for performing active biological operations of claim 64 wherein the collection electrode is a complexity reduction electrode.

67. An electronic device for performing active biological operations, comprising:

a support substrate having a first and second surface, and a via between the first and second surfaces to permit fluid flow through the substrate, the second surface supporting electrical traces,

a second substrate including at least a first surface, the first surface being adapted to be disposed in facing arrangement with the second surface of the first substrate, the second substrate including electrically conductive traces connecting to an array of microlocations, the array being adapted to receive said fluid through the via,

electrically conductive bumps interconnecting the electrical traces on the second surface of the support substrate and the electrical traces on the first surface of the second substrate,

a sealant disposed between the second face of the support substrate and the first face of the second substrate, said sealant providing a fluidic seal by and between the first substrate and the second substrate, and

a flowcell disposed on the first surface of the first substrate.

68. The electronic device for performing active biological operations of claim 67 wherein the support substrate is flex circuit.

69. The electronic device for performing active biological operations of claim 67 wherein the support substrate is a circuit board.

70. The electronic device for performing active biological operations of claim 67 wherein the second substrate is semiconductive substrate.

71. The electronic device for performing active biological operations of claim 67 wherein the electrically conductive bumps are solder.

72. The electronic device for performing active biological operations of claim 67 wherein the electrically conductive bumps are indium solder.

73. The electronic device for performing active biological operations of claim 67 wherein the electrically conductive bumps are conductive polymer.

74. The electronic device for performing active biological operations of claim 67 wherein the electrically conductive bumps are silver filled epoxy.

5 75. The electronic device for performing active biological operations of claim 67 wherein the sealant is a light curable polymer.

76. The electronic device for performing active biological operations of claim 75 wherein the light curable polymer is water-based.

10 77. An electronic device for performing active biological operations, comprising:

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a support substrate having a first and second surface, and a via between the first and second surfaces to permit fluid flow through the substrate,

15 a second substrate including at least a first surface, the first surface being adapted to be disposed in facing arrangement with the second surface of the first substrate, the second substrate including an array of microlocations, the array being adapted to receive said fluid,

a sealant disposed between the second face of the support substrate and the first face of the second substrate,

20 a source of illumination, and

a waveguide having an input adapted to receive the illumination from the source, and an output adapted to direct the illumination to the array, the waveguide being substantially parallel to the support substrate, the illumination from the waveguide illuminating the array.

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78. The electronic device for performing active biological operations of claim 77 wherein the source of illumination is a laser.

30 79. The electronic device for performing active biological operations of claim 78 wherein the laser is a laser bar.

80. The electronic device for performing active biological operations of claim 77 wherein the waveguide is affixed to the support substrate.

5 81. The electronic device for performing active biological operations of claim 80 wherein the waveguide is a polymer.

82. The electronic device for performing active biological operations of claim 77 wherein the source of illumination is a laser.

10 83. The electronic device for performing active biological operations of claim 77 wherein multiple waveguides are provided.

15 84. The electronic device for performing active biological operations of claim 77 wherein the support substrate is flex circuit.

85. The electronic device for performing active biological operations of claim 77 wherein the support substrate is a circuit board.

20 86. The electronic device for performing active biological operations of claim 77 further includes fluidics disposed on the first surface of the support substrate.

25 87. The electronic device for performing active biological operations of claim 77 further includes solder bumps between the support substrate and the second substrate.

30 88. A method for manufacturing a flip chip structure, the structure having a chip disposed adjacent a substrate, the substrate including a via therethrough, the structure being adapted to receive a fluid to be placed on the substrate, and to flow through the via down to the chip, at least a portion of the chip including an area to be free of sealant overcoat, comprising the steps of:

affixing a chip to a substrate,

providing a light curable, wickable sealant to the interface between the substrate and the chip,

exposing light to the device, onto the substrate, and through the via, down to the chip,

at least partially curing the sealant as a result of the exposure, whereby the sealant is precluded from flowing to said area to be free of sealant, and completing the cure of the sealant.

89. The method for manufacturing a flip chip structure of claim 88 wherein the sealant is curable.

90. The method for manufacturing a flip chip structure of claim 88 wherein the light is UV.

91. A system for the active electronic control of biological reactions in a multiple site environment comprising:

an array of unit sites,

a row selector operatively connected to the array for selective addressing of rows of the array,

a column selector operatively connected to the array for selective addressing of columns of the array,

an input adapted to receive unit site selection information, the input coupled to the row selector and the column selector,

current mirror circuitry for providing output current to the unit sites, and

power source connectors adapted to receive power and to supply power to the unit sites.

92. The system of claim 91 for the active electronic control of biological reactions wherein the row selector includes a memory.

93. The system of claim 92 for the active electronic control of biological reactions wherein the memory is a shift register memory.

94. The system of claim 93 for the active electronic control of biological reactions wherein the shift register is in a by one configuration.

95. The system of claim 91 for the active electronic control of biological reactions wherein the row selector includes a decoder.

96. The system of claim 91 for the active electronic control of biological reactions wherein the column selector includes a memory.

97. The system of claim 96 for the active electronic control of biological reactions wherein the memory is a shift register memory.

98. The system of claim 97 for the active electronic control of biological reactions wherein the shift register memory is in a by one configuration.

99. The system of claim 97 for the active electronic control of biological reactions wherein the shift register memory is in a by four configuration.

100. The system of claim 91 for the active electronic control of biological reactions wherein the column selector includes a decoder.

101. The system of claim 91 for the active electronic control of biological reactions further including a power source.

102. The system of claim 91 for the active electronic control of biological reactions further including a current mirror system.

103. The system of claim 91 for the active electronic control of biological reactions further including multiplexers for the alternative input of row and column selection.

5 104. A circuit for control of an output current in an active biological control reaction system, comprising:

a first column select transistor, the first column select transistor being adapted for control by a column selector,

10 a first row select transistor, the first column select transistor being adapted for control by a row selector, the first select transistors being connected in series to each other and between a node and a first supply,

an output connected to the node,

a second column select transistor, the second column select transistor being adapted for control by a column selector, and

15 a second row select transistor, the second row select transistor being adapted for control by a row selector, the second select transistors being connected in series to each other and between the node and a second supply.

20 105. The circuit of claim 104 for control of an output current in an active biological control reaction system wherein the output is directly connected to the node.

25 106. The circuit of claim 104 for control of an output current in an active biological control reaction system wherein the first row select transistor and the second row select transistor are CMOS transistors.

107. The circuit of claim 104 for control of an output current in an active biological control reaction system wherein the first and second column select transistors are CMOS transistors.

108. The circuit of claim 107 for control of an output current in an active biological control reaction system wherein the channel length of the column select transistors is larger than the channel length of the row select transistors.

5 109. The circuit of claim 104 for control of an output current in an active biological control reaction system further including a first test transistor spanning the first supply and the node.

10 110. The circuit of claim 109 for control of an output current in an active biological control reaction system wherein the first test transistor is adapted for control by a test signal. A

15 111. The circuit of claim 109 for control of an output current in an active biological control reaction system further including a second test transistor spanning the second supply and the node.

20 112. The circuit of claim 111 for control of an output current in an active biological control reaction system wherein the first test transistor is adapted for control by a test signal.

113. The circuit of claim 104 for control of an output current in an active biological control reaction system wherein the first supply is Vcc.

25 114. The circuit of claim 104 for control of an output current in an active biological control reaction system wherein the second supply is ground.

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